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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,712	10/10/2001	Carl Johan Friddle	LEX-0251-USA	7859

24231 7590 06/03/2004

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EXAMINER	
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ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/03/2004

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 052404

Application Number: 09/974,712
Filing Date: October 10, 2001
Appellant(s): FRIDDLE ET AL.

Lance Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 22, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1-3 and 5 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Skolnick, J. et al "From genes to protein structure and function:novel applications of computational approaches in the genomic era." Trends in Biotech, vol 18, no. 1 (2000), pp. 34-39

Bork, P. "Powers and pitfalls in sequence analysis:the 70% hurdle." Genome Research, vol. 10 (2000), pp. 398-400.

Doerks, T, et al. "Protein annotation:detective work for function prediction." Trends in Genetics, vol 14, No. 6 (June 1998), pp. 248-250.

Smith, TF, et al. "The challenges of genome sequence annontation or "the devil is in the details." Nature Biotechnology, vol. 15 (November 1997), p. 1222-1223.

Brenner, SE. "Errors in genome annotation." Trends in Genetics, vol. 15, No. 4 (April 1999), p. 132.

Bork, P. et al. "Go hunting in sequence databases but watch out for the traps." Trends in Genetics, vol. 12, No. 10 (October 1996), pp. 425-427.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3 and 5 are rejected under 35 U.S.C. 101. This rejection is set forth in prior Office Action mailed 12/17/02 and is reiterated in full below. These claims are directed to an isolated nucleic acid comprising SEQ ID NO:1, nucleic acid molecules which encode the protein of SEQ ID NO:2, and which hybridize to SEQ ID NO:1, or to the complement thereof. The Action states that the claimed receptor is what is termed an "orphan receptor" in the art. Appellants disclose in the specification that the receptor encoded for by the claimed nucleic acid molecule is believed to encode a protein (termed "NHP" for "novel human protein") related to voltage-gated potassium channels (page 2, lines 1-5). However, the disclosure in the specification that the receptor is homologous to these ion channels is not predictive of use. The specification discloses that the polynucleotide of the invention (SEQ ID NO:1) encodes a protein which is "shares structural similarity with mammalian...voltage-gated potassium channels." However, this is not a specific and substantial asserted utility, or a well established utility of the protein of the instant specification. No comparisons between the sequence of the protein of the present invention and any voltage-gated potassium channel protein have been disclosed in the specification, nor does the specification disclose that the protein encoded for by the polynucleotide of the present invention has biological activities similar to these channels. Sequence homology alone cannot be accepted in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation.

However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotide of the invention (SEQ ID NO:1) encodes a protein which is "shares structural similarity with mammalian...voltage-gated potassium channels." However, this is not a specific and substantial asserted utility, or a well established utility of the protein of the instant specification. No comparisons between the sequence of the protein of the present invention and any voltage-gated potassium channel protein have been disclosed in the specification, nor does the specification disclose that the protein encoded for by the polynucleotide of the present invention has biological activities similar to these channels. Sequence homology alone cannot be accepted in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (Trends in Biotech. 18:34-39, 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (Trends in Genetics 14:248-250, 1998) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (Nature Biotechnology 15:1222-1223, 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (Trends in Genetics 15:132-133, 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, most homologs must have different molecular and cellular functions. Finally,

Bork et al. (Trends in Genetics 12:425-427, 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Therefore, based on the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:1, which is only known to encode a protein which is similar to mammalian voltage-gated potassium channels.

Therefore, the instant claims are drawn to a nucleic acid molecule which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said nucleic acid molecule, or encoded protein, identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, or any significance of the nucleic acid molecule of the present invention, which has not been disclosed in the specification as having any specific or substantial utility, there is no immediately obvious patentable use for them. To employ the nucleic acid molecule of the instant invention to produce a receptor protein to identify substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for the nucleic acid molecule of the invention, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Therefore, since the nucleic acid molecule of the invention (SEQ ID NO:1), nor its encoded protein (SEQ ID NO:2), are supported by a specific and substantial asserted utility, or a well established utility, then polynucleotides encoding SEQ ID NO:2, as well as expression vectors comprising these nucleic acid molecule also do not possess utility.

(11) Response to Argument

In the Response dated 4/23/03, Appellants argue that the presently claimed sequence is clearly referred to as an ion channel protein in the title and specification. This argument has been considered, but is not deemed persuasive. Respectfully, though Appellants suggest that the sequence(s) of the present invention encodes ion channel proteins, this is speculative. There is no data to support this assertion. It cannot be concluded that the protein of the present invention is an ion channel simply because the specification states that it is believed to be an ion channel on the basis of homology alone.

Appellants argue that "an invention is useful under section 101 if it is capable of providing some identifiable benefit" and that "any utility of the claimed compounds is sufficient to satisfy 35 USC 101." However, as stated under the current utility guidelines (published 1/5/01, 66 FR 1092), the claimed invention needs to be supported by a specific and substantial asserted utility, or a well-established utility. However, no specific, or substantial benefit has been identified. The fact that these proteins "mediate or facilitate the passage of materials across the lipid bilayer" is not a utility specific to the protein of the present invention, as this is the general the function of voltage-gated ion channel proteins as a whole. Appellants have not taught what the specific function is of the protein encoded for by the nucleic acid molecules of the present invention, nor have Appellants identified a substantial role of this protein; for example, how this specific ion channel protein can be used, or with what diseases this specific protein is associated.

Furthermore, Appellants argue that Brenner v. Manson is not analogous to the present situation since an activity, such as an anticancer activity, is distinct from a term (i.e. ion channel) that defines a molecular function. Appellants argue that ion channels have a well-known biological role and that this description is more specific than a general "activity." However, the Examiner maintains that while these examples are not identical, they are, in fact, analogous. If the artisan were to consider "ion channel activity" to be analogous to "anticancer activity," as was intended in this analogy, then it can be seen how, simply because one protein or compound was known to have activity, this does not confer activity to other homologous proteins or compounds. Furthermore, the Examiner does not understand how these terms differ, i.e. how one is more general than the other. "Ion channel activity" is just as general or as specific as "anticancer activity." Both of these terms define a specific function (specific proteins which transport specific ions vs. specific drugs which affect specific cancer cells) as well as a general function (ion channels and the general concept of transporting ions vs. any drug which affects any cancer). Therefore, this situation, as well as the terms "ion channel activity" and "anticancer activity" are sufficiently analogous to be pertinent to this rejection. Even if, *arguendo*, these situations were not

analogous, homology alone is not a sufficient basis for a determination of utility, as discussed throughout this rejection.

Appellants further cite in *In re Brana*, their major argument being that "further research does not preclude a finding that the invention has utility" and that "further research and development" is (may be) necessary. However, In re Brana, as stated by Appellants, is concerned with the utility of *pharmaceutical compositions* whereas the present invention is concerned with ion channel *proteins*. In using Appellants' own logic, as seen in the above paragraph regarding Appellants' discussion of the relevance of Brenner v. Manson to the present invention, compounds (and pharmaceutical compositions) are not analogous to ion channel proteins. Appellants make no mention in their arguments of Brana that the compounds, themselves, to be used in the pharmaceutical compositions do not have utility. Appellants only state that Brana is concerned with the *pharmaceutical compositions* comprising these compounds. Appellants discuss the significance of the FDA and Phase II testing regarding Brana. However, these issues are not relevant in this situation. If Appellants were claiming that the protein of the present invention, or nucleic acids encoding this protein, could be used in pharmaceutical compositions, that would be analogous. However, the proteins themselves would first need to possess utility in order for the pharmaceutical composition to possess utility. Since the proteins of the present invention do not possess utility, any comparison to Brana is, respectfully, anappropriate.

On page 6 of the Appeal Brief dated 3/22/04, Appellants argue that it was asserted that the sequences of the present invention encode a novel mammalian ion channel protein (specification in title, on page 1, line 12 and on lines 24-28) that shares structural similarity with mammalian ion channel proteins, and particularly potassium channels and more particularly voltage-gated potassium channel proteins (specification on page 2, lines 2-4). Appellants further argue that the artisan would recognize the protein of the present invention as a KCNA7 variant since it shares 99.781% amino acid identity to GenBank AAK63002 and 99.9% mRNA identity to GenBank Accession No. AF315818. Appellants argue that the specification discloses tissues in which these sequences are expressed (heart and others at page 3, lines 31-34) and disease associations (particularly the cardiac related disorders high blood pressure, arrhythmia, and others at page 13, lines 22-24) both of which are consistent with the evidence provided in information provided in other scientific publications. Specifically, Appellants show that AF315818 encodes a voltage-gated potassium channel and that the reference citing this nucleic acid and protein (Bardien-Kruger et al.) teaches that this protein is believed to be involved in specific diseases, such as PFHBI. Appellants, therefore, argue that one skilled in the art would recognize the utility of the protein of Bardien-Kruger et al. as a utility of the protein of the present invention. However, Appellants

did not disclose the utility of the ion channel protein of the present invention at the time of filing. Utility has to have been present *at the time the invention was made (filed)*. Without knowing which cardiac disorders, or any other disorders, were associated with the protein of the present invention, the use of this protein, or encoding nucleic acid molecules, was not known at the time the invention was made. Post-filing references can only be used to support an assertion made in the specification at the time of filing. This is not the case here. As stated on page 4 of the Office Action dated 12/17/02, a patent is not a hunting license.

Appellants also argue that, according to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. 101 as allegedly lacking a patentable utility and under 35 U.S.C. 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA."

This argument has been considered, but is not deemed persuasive. First, unlike the Training Example, the claims of the present invention do not provide a function. Even, *arguendo*, it is assumed that the protein of the present invention is a potassium channel, the specific functions of this protein are not known. Potassium channels are expressed in a wide range of tissues and have numerous functions and can be associated with numerous diseases, unlike DNA ligase, who's sole function is to ligate DNA. Therefore, the artisan would know the specific function of a newly identified DNA ligase. However, knowing the specific function of a novel potassium channel is not as simple.

Appellants additionally argue that the references cited by the Examiner (Skolnick, Bork, Doerks, Smith, Brenner and Bork), if anything, support Appellants' assertion that homology can be used to predict the function of a novel protein, or encoding nucleic acid. All of Appellants' points regarding these references have been considered. Taken as a whole, these references show that prediction of novel proteins based on known homologous proteins is, at best, speculative. In addition, the issue raised by the Examiner is not that protein structure is not predictive of function, but that the standard in the art is that it is only suggestive, and needs to be confirmed by actual experimental results, which has not been done in the present situation. Therefore, homology alone is not a sufficient basis to conclude utility.

Appellants argue that naturally occurring genetic polymorphisms such as those described in the present specification are both the basis of, and critical to, inter alia, forensic genetic analysis and genetic analysis intended to resolve issues of identity and paternity and analysis based on identified polymorphisms is often used to convict or acquit in many criminal cases.

This argument has been considered, but is not deemed persuasive. The use of the claimed polynucleotides in a method of forensic analysis is not a specific utility because there is no correlation between the presence of any of the polymorphisms and any state or condition, and there is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder, therefore this asserted utility is not specific or substantial. Additionally, the Specification does not set forth the frequency with which these polymorphisms occur in the general population, thus the utility of the nucleic acid for forensic analysis is not complete since additional experimentation would be required. Such a utility is considered a research utility only designed to identify a particular function of the claimed sequences and is not a substantial utility. See, e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility."

Furthermore, Appellants argue that the nucleic acid molecules of the present invention can be used in gene (DNA) chips and that these chips have substantial industrial utility. They also argue that the protein of the present invention is a G protein-coupled receptor, and, therefore, is a potential drug target and specific marker of the human genome, for chromosome mapping, or for defining exon-splice junctions. Appellants also state that "the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the...arts." However, none of these assertions are specific to the protein of the present invention, or its encoding nucleic acids. Any nucleic acid can be used in gene chip technology, or as a marker for a specific location on the human genome and the like. Similarly, hundreds of G protein-coupled receptors are known in the art and are used as drug targets. Again, this is not specific to the protein of the present invention. As made in a similar statement above, the fact that this nucleic acid molecule maps to chromosome 19q13.3 was not disclosed at the time of filing, nor does this knowledge provide any specific or substantial information regarding this chromosome, or the nucleic acid molecule. The argument that the nucleic acid of the present invention is part human genome project is also not persuasive since, while the human genome project as a whole may be useful, a single nucleic acid molecule, such as the one disclosed in this invention, by itself, is not.

Finally, Appellants bring to the Examiner's attention numerous patents on polynucleotide sequences that have not been directly shown to be associated with the function of the protein set forth in the specification and which claim, for example, polynucleotide fragments. These arguments have been considered, but are not persuasive. First, this application was properly examined under, and is consistent with, the current utility guidelines, published 1/5/01, 66 FR 1092. Furthermore, all U.S. Patent are presumed valid, or would not have issued as U.S. Patents. It is believed that all pertinent arguments have been addressed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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PATENT EXAMINER

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June 1, 2004

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